Chapter 1

Summary

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INTRODUCTION

At the 2012 World Health Assembly, member states agreed to a goal of reducing rates of premature death from noncommunicable diseases (NCDs) by 25 percent by 2025, starting from a 2008 baseline (WHO 2011a, 2011b). The United Nations (UN) Sustainable Development Goals for 2030, announced in September 2015, will include reducing premature death from NCDs, of which cancer is a substantial part (map 1.1).

This chapter summarizes the analyses and conclusions of the 79 authors of this volume on cancer, *Disease Control Priorities, 3rd edition* (*DCP3 Cancer*), and analyzes interventions for effectiveness, cost-effectiveness, affordability, and feasibility in low- and middle-income countries (LMICs; see box 1.1 for key messages). The intent is to help governments of LMICs commit to locally appropriate national cancer control strategies that will include a range of cost-effective interventions, customized to local epidemiological patterns and available funding, and to convey this commitment widely to their populations. Where affordable treatment can be provided, conveying this to the public can motivate people to seek treatment when their cancer is at an earlier, much more curable stage. Providing a package of services that addresses a large part of the cancer burden will go a long way toward helping countries reach the new NCD goals. *DCP3 Cancer* is one of nine planned volumes in the *DCP3* series (box 1.2).

The *DCP3* package includes prevention strategies, but many cancers cannot be prevented to any great extent by available methods. Some can be treated effectively (breast and childhood cancers, for example), however, and the availability of effective treatment bolsters public confidence in the overall program (Brown and others 2006; Knaul and others 2011; Sloan and Gelband 2007). Cancer control programs can mobilize broad political support, as happened in Mexico with the addition of breast cancer and childhood cancer treatment into expanded national health insurance coverage (Knaul and others 2012).

In high-income countries (HICs), most who develop cancer survive, although survival depends strongly on the type of cancer (table 1.1). In LMICs, less than one-third survive, and in some the proportion is much smaller (Ferlay and others 2015). The differences in survival are due partly to differences in the patterns of cancer incidence; some types of cancer that are common in many LMICs, such as lung, esophagus, stomach, and liver cancers, have a poor prognosis even in HICs (Bray and Soerjomataram 2015, chapter 2 in this volume). The other major contributor to poor outcomes is that many fewer people come for treatment when their cancer is at an early, curable stage than in HICs (Allemani and others 2015; Ferlay and others 2015).

The aim of *DCP3* is to identify cost-effective, feasible, and affordable interventions that address significant

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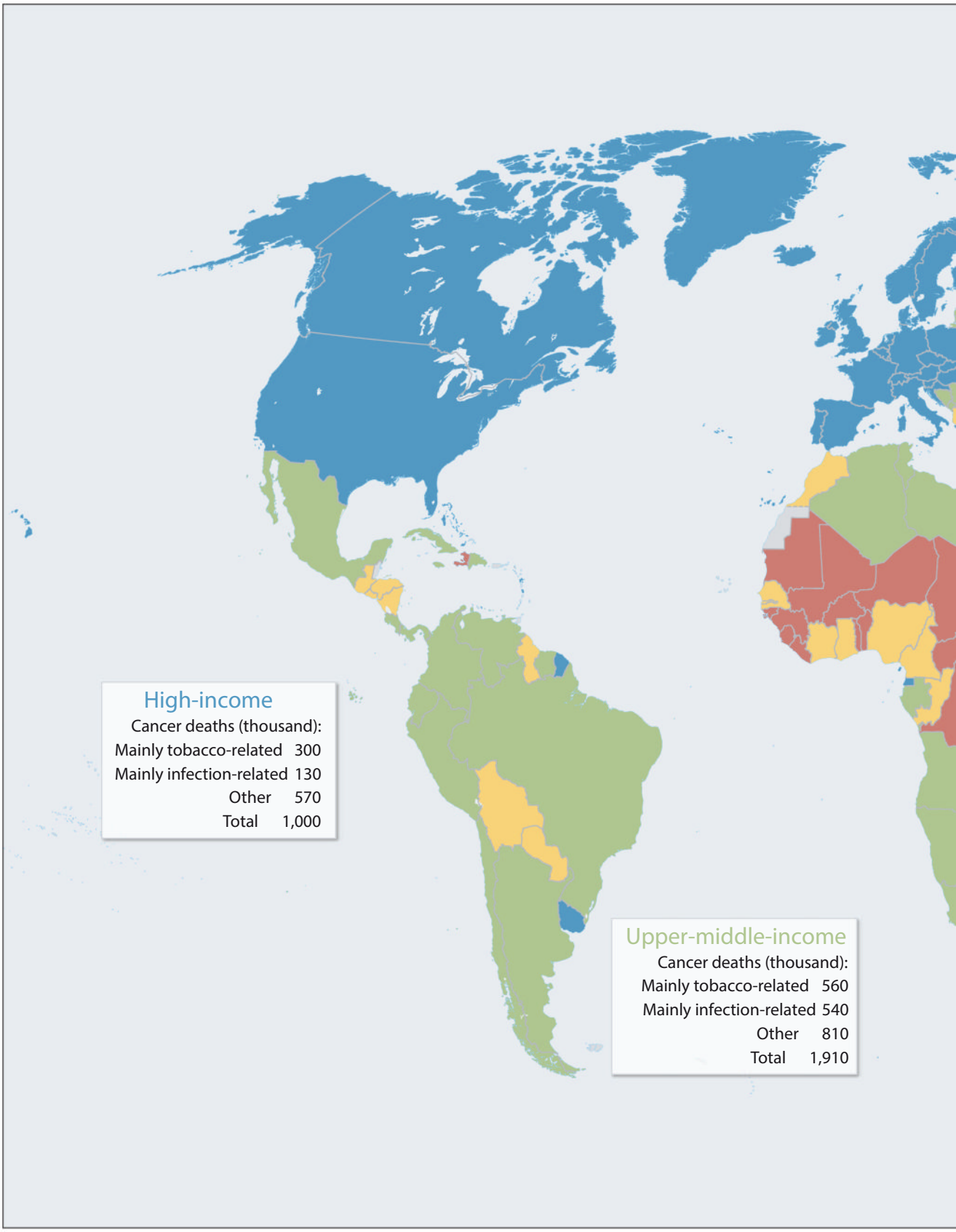
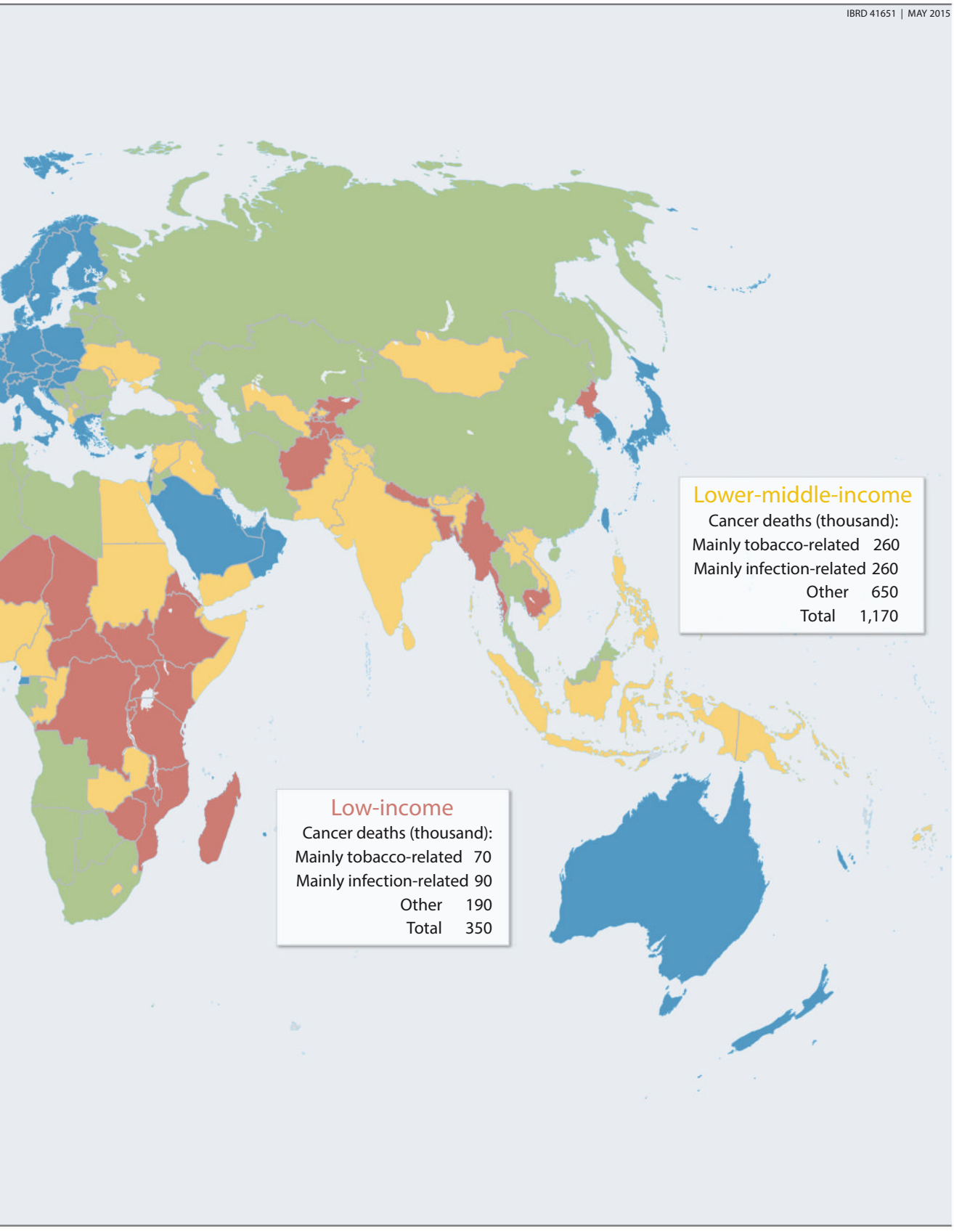
MAP 1.1 Cancer Mortality Before Age 70 Years, by World Bank Income Groupings, 2012



Source: Based on WHO Global Health Estimates (WHO 2012)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Lower-middle-income
Cancer deaths (thousand):
Mainly tobacco-related 260
Mainly infection-related 260
Other 650
Total 1,170
Low-income
Cancer deaths (thousand):
Mainly tobacco-related 70
Mainly infection-related 90
Other 190
Total 350

Box 1.1

Key Messages

Cancer is already a major cause of death in low- and middle-income countries (LMICs), particularly in middle-income countries, and will increase as a percentage of deaths in all LMICs, driven by population aging and faster declines in other causes of death.

In most populations, helping current tobacco users to quit and young people not to start smoking are the most urgent priorities in cancer prevention (and in the control of other noncommunicable diseases), along with vaccination against hepatitis B and the human papillomavirus (HPV). Higher tobacco taxes and accompanying interventions will reduce cancer incidence and generate substantial extra revenues for governments.

Other than tobacco- and virus-related cancers, however, most of the increase in cancer incidence is not currently preventable, but many cases of cancer can be effectively treated. Early breast cancer and cervical cancer are common, and often curable; precancerous cervical lesions are even more curable. Childhood cancers are relatively rare, but some are highly curable. The interventions supported by the analyses in this *Disease Control Priorities, 3rd edition* (*DCP3 Cancer*) go beyond current World Health Organization best buys, which are limited to interventions that are deliverable in primary care settings.

The *DCP3* essential package of cost-effective and feasible interventions would, if fully implemented, cost an additional $20 billion per year, or 3 percent of total public spending on health in LMICs; 2.6 percent in upper-middle-income countries (UMICs); and 5 percent in lower-middle-income countries; but 13 percent in low-income countries (LICs). In per capita terms, this would cost $5.70, $1.70, and $1.70 annually in UMICs, lower-middle-income, and LICs, respectively. Such increases are potentially feasible in all but the LICs, which would require external support.

Cancer services that are considered appropriate for a national cancer strategy should be covered through universal health coverage as soon as countries are able to do so.

Global initiatives for cancer control in LMICs are needed to lower the costs of key inputs for the essential package, including large-scale commodity purchases; to expand technical assistance; and to promote cancer research.

disease burdens in LMICs (box 1.3). Accordingly, we have examined the following:

1. The avoidable burden of premature death (defined as before age 70, which approximates current global life expectancy) from cancer in LMICs (table 1.1)
2. The main effective interventions for the prevention, early detection, treatment, and palliation of cancer, and their cost-effectiveness
3. The costs and feasibility of developing health system infrastructure that could deliver progressively wider coverage of a set of cost-effective cancer services.

Using these inputs, we define an "essential package" of cost-effective interventions for cancer and discuss their affordability and feasibility, which differ markedly between low-, lower-middle-, and upper-middle-income countries. Even within the same income categories, countries may differ widely in epidemiological patterns and health systems, resulting in different country-specific essential packages. Hence, this is not intended to lead to a common cancer plan for all LMICs, but to identify elements that will be appropriate in many countries and spur discussion within countries about rational cancer control planning and implementation. The result would be national cancer plans that are tailored to local conditions but retain the characteristics of effectiveness, cost-effectiveness, feasibility, and affordability. Finally, we review some ways in which global initiatives could help LMICs to expand cancer control.

Box 1.2

From the Series Editors of Disease Control Priorities, 3rd Edition

Budgets constrain choices. Policy analysis helps decision makers achieve the greatest value from limited available resources. In 1993, the World Bank published *Disease Control Priorities in Developing Countries* (*DCP1*), an attempt to assess systematically the cost-effectiveness (value for money) of interventions that would address the major sources of disease burden in low- and middle-income countries [Jamison and others 1993]). The World Bank's 1993 *World Development Report* on health drew heavily on the findings in *DCP1* to conclude that specific interventions against noncommunicable diseases were cost-effective, even in environments in which substantial burdens of infection and undernutrition persisted.

DCP2, published in 2006, updated and extended *DCP1* in several respects, including explicit consideration of the implications for health systems of expanded intervention coverage (Jamison and others 2006). One way that health systems expand intervention coverage is through selected platforms that deliver interventions that require similar logistics but address heterogeneous health problems. Platforms often provide a more natural unit for investment than do individual interventions, and conventional health economics has offered little understanding of how to make choices across platforms. Analysis of the costs of packages and platforms—and of the health improvements they can generate in given epidemiological environments—can help guide health system investments and development.

DCP3 differs substantively from *DCP1* and *DCP2* by extending and consolidating the concepts of platforms and packages and by offering explicit consideration of the financial risk protection objective of health systems. In populations lacking access to health insurance or prepaid care, medical expenses that are high relative to income can be impoverishing. Where incomes are low, seemingly inexpensive medical procedures can have catastrophic financial effects. *DCP3* offers an approach that explicitly includes financial protection as well as the distribution across income groups of the financial and health outcomes resulting from policies (for example, public finance) to increase intervention uptake (Verguet, Laxminarayan, and Jamison 2015). The task in all the volumes has been to combine the available science about interventions implemented in very specific locales and under very specific conditions with informed judgment to reach reasonable conclusions about the impacts of intervention mixes in diverse environments. The broad aim of *DCP3* is to offer, for consideration and adaptation, essential intervention packages—such as the essential cancer package in this volume—and their related delivery platforms. This information will assist decision makers in allocating budgets so that health system objectives are maximally achieved.

The nine volumes of *DCP3* are being published in 2015 and 2016 in an environment in which serious discussion continues about quantifying the sustainable development goal (SDG) for health (UN 2015). The analyses in *DCP3* are well-placed to assist in choosing the means to attain the health SDG and assessing the related costs. The final volume will explore SDG-related and other broad policy conclusions and generalizations, based on the analytic findings from the full set of volumes. Each individual volume will provide valuable, specific policy analyses on the full range of interventions, packages, and policies relevant to its health topic.

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Table 1.1 Worldwide Cancer Deaths in 2012 at Ages 0–69 by Cancer Site and Country Income Grouping, and 5-Year Survival Rates in Low-, Middle-, and High-Income Countries

	Annual Deaths, age 0–69 years (thousands) by World Bank country income group					5-year survival (%), cancer registry data	
Population in billions Cause of cancer and other deaths	Low income 0.8	Lower-middle income 2.4	Upper-middle income 2.3	High income 1.2	World (total) 6.7	Low or middle income 5.5	High income 1.2
Cancer, by site (ICD-10 C00-99)							
Lung, mouth, and esophagus	70	260	560	300	1,200	10	20
Liver	30	90	270	60	440	10	20
Breast	30	140	110	80	360	75	90
Stomach	20	80	210	50	360	20	40
Colon or rectum	20	80	120	100	310	50	60
Cervix	40	90	60	20	200	55	65
Ovary	8	30	30	30	100	25	40
Leukemia, age 0–14 years	3	10	10	2	30	65	90
age 15–69 years	10	40	60	30	140	30	50
Prostate	4	10	20	20	60	70	90
Other/unknown site	110	330	470	310	1,220	—	—
All cancers (% of all causes)	**350 (6%)**	**1,170 (6%)**	**1,920 (22%)**	**1,000 (37%)**	**4,400 (14%)**	—	—
All noncommunicable diseases	**1,660**	**6,300**	**5,950**	**2,200**	**16,070**	—	—
Communicable/external causes	**4,100**	**7,380**	**2,650**	**500**	**14,660**	—	—
All causes	**5,760**	**13,680**	**8,600**	**2,700**	**30,730**	—	—

Sources: Population and mortality based on data from the UN Population Division (UNPD 2012) and WHO Global Health Estimates (WHO 2012). Estimated 5-year survival based on Allemani and others 2015.
Note: Number of deaths above 10,000 are rounded to the nearest 10,000, so totals may differ. Estimated five-year survival rounded to the nearest 5 percent. — = Not applicable.

EVOLVING CANCER BURDEN

The WHO's International Agency for Research on Cancer (IARC) estimates that in 2012 there were 14 million new cases of cancer and 8 million deaths from cancer, more than half of them in people younger than age 70 years (table 1.1) (Ferlay and others 2015). Of the 4.4 million cancer deaths before age 70, 3.4 million were in LMICs; 1.9 million in UMICs, 1.2 million in lower-middle-income countries, and 0.3 million in LICs. Two-thirds of the cancer deaths before age 70 years in LMICs were cancers of the lung, mouth, or esophagus (0.9 million, many caused by tobacco), liver (0.4 million, many caused by vaccine-preventable hepatitis B infection), stomach (0.3 million), breast (0.3 million), cervix (0.2 million, many caused by human papillomavirus [HPV] infection), and colon or rectum (0.2 million) (See table 1.1, figure 1.1; and Bray and Soerjomataram 2015; Ferlay and others 2015; WHO 2012).

Worldwide, cancer death rates are slowly decreasing (table 1.2). Between 2000 and 2010, age-standardized cancer death rates before age 70 years fell by about 1 percent per year, bolstered by worldwide declines in cervical cancer and stomach cancer, for reasons that are not fully understood. Male lung cancer rates decreased in some countries, but in lower-middle-income countries, the death rates from tobacco-associated cancers rose slightly.

Absolute numbers of cancer deaths and cancer as a proportion of all deaths will continue to rise because of three factors: world population is increasing, particularly in later middle age and old age; mortality from diseases other than cancer is decreasing; and in some major populations the effects of tobacco are

Box 1.3

Methods

The 79 authors of the 18 chapters in this volume surveyed the published and gray literature to identify cost-effective interventions for the cancers studied. Cancer-specific incidence and mortality data are from the International Agency for Research on Cancer's GLOBOCAN (Ferlay and others 2015). Mortality data are from the World Health Organization's Global Health Estimates (WHO 2012), and demographic estimates are from the United Nations (UNPD 2012).

The analyses were stratified by World Bank country group classifications as defined by 2013 per capita gross national income: 34 low-income countries (less than US$1,045), 50 lower-middle-income countries (US$1,046 to US$4,125), and 55 upper-middle-income countries (US$4,126 to US$12,745) (World Bank 2014a).

Cost-effectiveness estimates were compiled for each cancer and each intervention. Systematic searches were conducted in PubMed for all interventions covered in the volume, for studies in or including low- and middle-income countries (LMICs), published in 2003–13 (Horton and Gauvreau 2015). For colorectal cancer, studies from high-income Asian economies were also sought. A recent review of the cost-effectiveness of cancer interventions for high-income countries (HICs) was also useful (Greenberg and others 2010). The studies identified used various outcome measures: life years saved, quality-adjusted life years (QALYs) gained, and disability-adjusted life years averted. Evidence from studies in LMICs was preferred, but rarely available. Evidence from HICs was considered in all cases, and evidence from high-income Asian economies was particularly important. We adopted the scale used by the Commission on Macroeconomics and Health (2001) to define very cost-effective, cost-effective, and cost-ineffective as costing < 1, 1–3, and > 3 times per capita income per QALY (or other measure), respectively. (Commission on Macroeconomics and Health 2001).

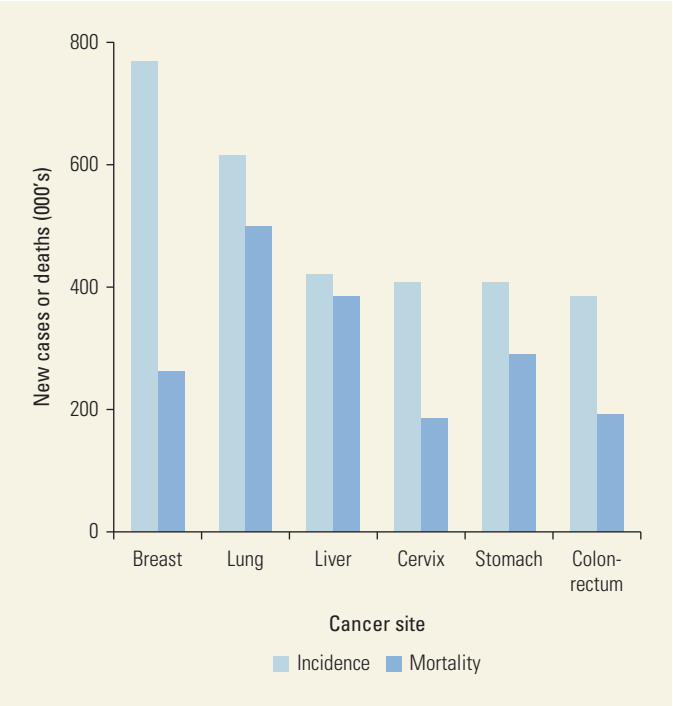
The essential package includes interventions rated as very cost-effective and cost-effective and considered potentially affordable and feasible in resource-constrained environments. Costs are expressed in 2012 prices. Costs are also expressed as a percentage of national public spending on health, estimated by the World Bank (World Bank 2014b).

increasing (Jha 2009). Based on population growth alone (at 2010 death rates age-standardized to the expected 2030 population), more than 6 million cancer deaths are expected in 2030 in people younger than age 70 years, and an equal number in people age 70 years and older (table 1.3). Three-quarters of these future cancer deaths are expected to occur in middle-income countries (MICs).

IMPACT ON HOUSEHOLDS

Counter to common perceptions, cancer death rates are often higher in lower-income groups than high-income groups. In India, the age-standardized death rate from cancer in middle age was twice that in illiterate as in educated populations (Dikshit and others 2012). As are other NCDs, cancer is an important cause of catastrophic health expenditures that can push households into poverty (Hamid, Ahsan, and Begum 2014; Hoang Lan and others 2013; Ilbawi, Einterz, and Nkusu 2013; John and others 2011), because in many LMICs, cancer surgery, radiotherapy, and chemotherapy are paid for largely out of pocket. In Bangladesh (Hamid, Ahsan, and Begum 2014) and Cameroon (Ilbawi, Einterz, and Nkusu 2013), for example, high user fees increase the likelihood that patients will not return at all for cancer surgery. Conversely, in India, some standard types of cancer surgery (for example, mastectomy) are supposed to be provided at low, affordable cost in public hospitals; in China, the national health insurance scheme now offers standard types of cancer surgery at prices most people can afford. Nevertheless, even in China and India, cancer can still impose a major financial burden on families, especially in the lowest income groups, and in the case of India, cancer services are limited to certain large cities (Mallath and others 2014). An objective of *DCP3* is to evaluate interventions for their distributive effects, with particular emphasis on the effects on the poor and on impoverishment at any economic level because of health care expenses.

Figure 1.1 Incidence and Mortality of Selected Cancers before Age 70 Years, Low- and Middle-Income Countries, 2012



Source: Based on IARC GLOBOCAN data (Ferlay and others 2015).

ESSENTIAL PACKAGES OF INTERVENTIONS

The *DCP3* essential package of interventions for cancer is intended to be considered and modified as appropriate by governments. The specific interventions and the criteria used to choose them (effectiveness, cost-effectiveness, feasibility, and affordability) are intended to help LMIC governments decide what to support and what not to support (Jamison 2015).

For MICs that already have cancer treatment centers and clinics, the *DCP3* approach could be used to help evaluate additional interventions, now or in the future, or to re-assess some current activities; in all LMICs it could help ensure due consideration of how interventions that are considered locally appropriate can achieve high population coverage.

The WHO has formulated a list of NCD best buys for LMICs, which were limited to services considered feasible at the primary care level. Those most relevant to cancer are three preventive measures: a set of tobacco control interventions, hepatitis B vaccination to prevent liver cancer, and some form of screening and treatment for precancerous cervical lesions (WHO 2011b). The *DCP3 Cancer* essential package (table 1.4) adds HPV vaccination (also included by the Commission on Investing in Health [Jamison and others 2013]) to prevent cervical cancer. The *DCP3* also adds treatment of early-stage cervical cancer (Denny and others 2015, chapter 4 in this volume); diagnosis and treatment for early breast cancer (Anderson and others 2015, chapter 3 in this volume); diagnosis and treatment for selected, highly curable childhood cancers (Gupta and others 2015, chapter 7 in this volume); and palliative care (Cleary, Gelband, and Wagner 2015, chapter 9 in this volume), including, at a minimum, opioid drugs for severe pain control. Treating early stage breast and cervical cancer includes quality surgery, which could also be available for many other early-stage resectable cancers. The package is organized according to delivery platforms, classified as national level policy, regulation, or community information; primary health clinic or mobile outreach; first-level hospital; or specialized cancer center.

The cost of the essential package is estimated for the entire population, not restricted to age under 70 years. We estimated the global and per capita costs of each intervention in the package separately for low-income,

Table 1.2 Changes in Deaths from All Causes and Cancer, by Country Income Group, Ages 0–69, 2000–10
(Percent change in mortality rate)

	Change in % 2000–10 by World Bank country income group				
Cause of death	**Low-income**	**Lower-middle-income**	**Upper-middle-income**	**High-income**	**World**
All cancers	–6	–2	–12	–13	**–10**
Lung, mouth, esophagus (mainly tobacco-related)	–6	+1	–11	–12	**–9**
Cervix, liver, stomach (mainly infection-related)	–13	–2	–18	–24	**–15**
All other cancers	–4	–3	–9	–12	**–8**
All causes	–21	–15	–23	–17	**–19**

Sources: Based on data from IARC GLOBOCAN (Ferlay and others 2015) and WHO Global Health Estimates (WHO 2012).

Table 1.3 Projected Deaths from All Causes and Cancer at Ages 0–69 Years, 2030
(at 2010 death rates, thousands)

Population/Cause of death	Low-income	Lower-middle-income	Upper-middle-income	High-income	World
All Causes	8,620	18,110	11,600	2,960	41,290
Cancer	590	1,690	2,690	1,130	6,100
Lung, mouth, esophagus	130	390	820	350	1,690
Cervix, liver, and stomach	80	250	700	120	1,150
All other cancers	380	1,050	1,170	660	3,260

Sources: Based on data from UNPD 2012 and WHO Global Health Estimates (WHO 2012).
Note: All deaths are rounded to nearest 10,000. All cancer deaths (in thousands) at ages 70+ would be 240, 800, 3,110, 2,450, and 6,600 in low-income countries, lower-middle-income countries, upper-middle-income countries, high-income countries, and worldwide, respectively.

Table 1.4 Essential Cancer Intervention Package[a]

Cancer type/ Number of deaths, ages 0–69 years, 2012 (thousands)	Platform for intervention delivery			
	Nationwide policies, regulation, or community information	Primary health clinic or mobile outreach	First-level hospital[b]	Specialized cancer center/unit[c]
All cancers **3,230**	Education on tobacco hazards, value of HPV and HBV vaccination, and importance of seeking early treatment for common cancers Palliative care, including, at a minimum, opioids for pain relief[d]			
Selected tobacco-related cancers (oral, lung, and esophagus) **900**	Taxation; warning labels or plain packaging; bans on public smoking, advertising, and promotion; and monitoring	Cessation advice and services, mostly without pharmacological therapies		
Breast cancer **280**				Treat early-stage cancer with curative intent[e]
Cervical cancer **180**	School-based HPV vaccination	Opportunistic[f] screening (visual inspection or HPV DNA testing); treat precancerous lesions	Treat pre-cancerous lesions	Treat early-stage cancer
Colorectal cancer **210**			Emergency surgery for obstruction	Treat early-stage cancer with curative intent
Liver cancer **380**		Hepatitis B vaccination (including birth dose)		
Childhood cancers **80[g]**				Treat selected early-stage cancer with curative intent in pediatric cancer units/hospitals

Note: Cancer totals are rounded to nearest 10,000. Education and basic palliative care are relevant for cancers at all ages. HBV = hepatitis B virus; HPV = human papillomavirus.
a. Red type denotes emergency care.
b. First-level hospitals are referred to as district hospitals in some countries.
c. Some interventions may take place at first-level hospitals, by a specialized surgeon visiting once per month, for example.
d. Palliative care should be available at all levels specified in the table and in the home.
e. Early-stage cancer generally refers to stages I and II.
f. Screening is opportunistic when a test is requested by a patient or offered by a practitioner to a patient attending for another reason. Organized screening is a well-defined process including formal invitations to participate, recalls, reminders, tracking results, ensuring follow-up, monitoring, and reporting program performance results.
g. Including some solid tumors.

lower-middle-income, and upper-middle-income countries. Most LMICs should be able to implement a locally customized essential package that covers most of their population by 2030, given anticipated increases in public spending on health (Jamison and others 2013). The schedule of implementation will vary, however, as some interventions—in particular, higher tobacco taxes and widespread pain palliation—can begin rapidly in many countries (Foley and others 2006; Sloan and Gelband 2007). By contrast, affordable availability of treatments that require considerable infrastructure development may take many years to achieve fully after a start is made.

Prevention

Most countries (183 worldwide) now vaccinate infants against hepatitis B, with global coverage estimated at 81 percent in 2013. This will prevent many liver cancers some decades hence, but a birth dose, particularly important in countries with high mother-to-child transmission, reached only 26 percent of newborns in 2011 (WHO 2011c).

Seventy-five countries (including HICs) have begun national HPV vaccination programs and others are developing experience with the vaccine (Gavi 2013). In addition, Gavi, the Vaccine Alliance, is supporting pilot programs in several LICs in Sub-Saharan Africa. The delivery cost of reaching adolescent girls with three doses is the major barrier, as Gavi-subsidized vaccine costs only US$0.20 to US$0.40 per dose, while program costs range between US$4 and US$13 per fully immunized girl (Denny and others 2015; Gavi 2013). Hepatitis B and HPV vaccinations will have their main effect on mortality during the second half of the century, when the cohorts of immunized children reach middle age.

Tobacco control, notably much higher tobacco excise taxes (which result in marked increases in adult cessation), can have a more immediate effect: people who quit smoking before age 40 years avoid more than 90 percent of the risk they would have incurred had they continued to smoke (Jha and Peto 2014). This means a substantial saving of lives starting within 5–10 years after measures are put in place. Higher cigarette taxes also discourage youth initiation, which will prevent many deaths in the second half of the century. However, cessation remains uncommon in most LMICs, with adults quitting often as a result of cancer and other diseases, and not to avoid them. Only 28 countries are undertaking comprehensive tobacco control programs that include high taxes as a major strategy (WHO 2013). There are already some notable successes: France and South Africa used large tax increases in the 1990s to triple the price of cigarettes; by 2005, consumption had halved, but government revenues from tobacco had doubled (Van Walbeek 2005). In France, lung cancer mortality among young adults fell shortly after the tax was raised. Brazil has also reduced smoking prevalence considerably (Monteiro and others 2007). Despite severe industry opposition, Mexico, and very recently, India and the Philippines, have levied notable increases in cigarette taxes, and in Mexico cigarette sales have already started to decline (Jha and others 2015, chapter 10 in this volume; WHO 2013). The WHO's Framework Convention on Tobacco Control, adopted by more than 180 countries, is an important enabler of country action on tobacco (Jha 2015).

Screening

The emphasis on diagnosing and treating cancers while they are still at an early stage might suggest the appropriateness of many cancer screening programs (Sullivan, Sullivan, and Ginsburg 2015, chapter 12 in this volume), but population screening is expensive (even if cost-effective, at least in some populations in HICs) and requires considerable infrastructure. Only opportunistic cervical screening (with or without some added outreach) meets the *DCP3* criteria and is a suggested component of an essential package. Screening using visual inspection with acetic acid (which makes abnormal tissue appear white) can detect precancerous lesions that can be treated inexpensively (often during the same visit) to prevent cervical cancer from developing (Denny and others 2015; Goss and others 2013). When convenient, rapid diagnostic tests for the main carcinogenic types of HPV infection become affordable and available for use by fieldworkers, they could make such screening much more effective and reliable (Sankaranarayanan and others 2009). Two or three such screenings per lifetime, starting around age 35 years, at intervals of five to10 years, should reduce lifetime cervical cancer risk by more than half (Goldie and others 2005).

The essential package does not include any type of screening for prostate or breast cancer. Both have attracted significant controversy in HICs, although for different reasons. The most widespread means of prostate cancer screening is through a blood test for prostate-specific antigen (PSA, a protein produced at elevated levels by cancerous prostate cells), with or without digital rectal examination. Although it is a simple test, PSA is not supported by national programs because it leads to overdiagnosis and overtreatment, with many more men harmed by the side effects of overtreatment than are saved from prostate cancer. The U.S. Preventive Services Task Force discourages

PSA testing (U.S. Preventive Services Task Force 2012). By contrast, screening mammography for breast cancer is supported by most HICs as an expensive but moderately effective measure, although the optimal age range for screening and screening frequency are still debated. Clinical breast examination might be a viable option in LMICs, but the effectiveness of this requires more research (Anderson and others 2015). Other common cancers with detectable precancerous stages are colorectal cancer (precancerous polyps) (Rabeneck and others 2015, chapter 6 in this volume) and oral cancer (visible lesions) (Sankaranarayanan and others 2015, chapter 5 in this volume). Eventually, screening for more cancers may be added, but it is likely to be appropriate after effective treatment is established.

Diagnosis and Treatment

Accurate diagnosis is needed for cancer treatment, but shortages of trained pathologists and other laboratory technologists and lack of facilities and supplies critically limit diagnostic capacity in many LMICs (Gospodarowicz and others 2015, chapter 11 in this volume). In addition to an initial diagnosis of cancer (often based on biopsy specimens) that can help in assessing the need for major surgery, diagnostic services can help determine treatment strategies after surgery. The status of tumors, nodes, and metastases has long been clinically useful, and other tests on the tumor itself can determine post-surgical management. In particular, breast cancer surgical specimens should undergo reliable testing to see if they carry the estrogen receptor protein; if they do (that is, if the tumor is ER+), endocrine treatment will substantially reduce the risk of recurrence and death (box 1.4).

Treatment for early breast cancer and cervical cancer includes some or all of the following: surgery, radiotherapy, chemotherapy, and targeted (for example, endocrine) therapy, that is, all the basic components of cancer care (Anderson and others 2011; Knaul and others 2011). For early cervical cancer, surgery is the primary treatment and radiotherapy is an adjunct. For whatever is considered complete treatment in a given country context, all components of care should be accessible by patients once treatment is started. Partial or incomplete treatment can cause side effects, but with less chance of clinical benefit.

Childhood cancer is rare (accounting for 1 percent of cancer deaths in HICs), representing by far the smallest burden of the cancers targeted by the essential package. Although they cannot be prevented, many common childhood cancers have high cure rates in HICs, making them feasible targets (Gupta and others 2015). Cure rates in most LMICs are far lower, but reasonably good outcomes have been achieved in specialized childhood cancer centers and through national referral and management plans, particularly for acute lymphoblastic leukemia, Burkitt lymphoma, and Wilms tumor (Gupta and others 2014).

Palliative Care

Many incurable cancers cause intractable pain. Opioid medications can generally relieve this pain, greatly improving the quality of the last few weeks or months of life for patients and families. The simplest and least expensive preparation, oral morphine, works for an estimated 90 percent of patients with severe terminal cancer pain (Foley and others 2006). It is also used by patients with HIV/AIDS and some other chronic conditions. Palliative care is widely available only in HICs, but it could be made available in LMICs quite rapidly, even before other types of treatment. Palliative care includes more than pain control and is relevant throughout the course of illness, but pain control is the core and the greatest need is at the end of life.

With appropriate organization and cooperation from the government and the health care sector, opioids can be provided even in rural areas, at home, at low cost. The current reality is, however, that few people have access to effective pain medicines because of unnecessary and ill-conceived restrictions at the country level. In 2006 (with only marginal progress since then), 66 percent of the world's population lived in countries that had virtually no consumption of opioids, 10 percent in countries with very low consumption, 3 percent in countries with low consumption, and 4 percent in countries with moderate consumption (Seya and others 2011).

Local Priority Conditions

The essential package can be customized and augmented with locally appropriate and feasible interventions. Examples include improved storage of grain and other foods to avoid fungal contamination that contributes to high liver cancer rates in parts of Africa and Asia (Gelband and others 2015, chapter 8 in this volume; Groopman, Kensler, and Wild 2008); opportunistic screening (especially of high-risk tobacco users) and treatment for precancerous lesions and early-stage oral cancer in India and other countries with high oral cancer burdens (Dikshit and others 2012; Sankaranarayanan and others 2015); screening and treatment for colorectal cancer in Argentina and Uruguay (Goss and others 2013; Rabeneck and others 2015); and elimination of liver flukes (with the drug praziquantel) to prevent bile duct cancer in the limited areas where flukes are common,

Box 1.4

Possible Strategies for Treating Early Breast Cancer in LMICs

By definition, in early breast cancer (stage I or II), all detectable disease can be removed surgically, but micrometastases may remain that, perhaps years later, cause recurrence and death. Adjuvant treatments may be given after surgery to reduce this risk. In high-income countries, most women receiving appropriate treatment for early breast cancer survive their disease (Early Breast Cancer Trialists' Collaborative Group and others 2012). The success rate of breast-conserving surgery (lumpectomy) plus radiotherapy to the conserved breast is about the same as for mastectomy (removal of the entire breast, and perhaps some local lymph nodes) and either can be offered, if safe radiotherapy is available. The most basic surgical procedure for stage II breast cancer is some form of mastectomy (Anderson and others 2015). In low- and middle-income countries (LMICs), for women with early breast cancer, the first requirement is good quality, safe surgery. In low-income countries (LICs), in particular, timely access to safe surgery is a major barrier. In middle-income countries (MICs), where there is generally better population access to surgical services, *quality* cancer surgery is the major surgical concern, particularly adequate resection of the tumor (Dare and others 2015). After technically successful surgery, treatments can be based on estrogen-receptor (ER) status, estimated recurrence risk, and general health (Anderson and others 2015).

The ER status of surgically removed breast cancers can be determined (for about US$10, in India). If the cancer is ER-positive, about five years of endocrine drug therapy substantially reduces the 15-year recurrence risk and is relatively nontoxic. Endocrine drugs, such as tamoxifen or, for post-menopausal women, an aromatase inhibitor (AI) (Early Breast Cancer Trialists' Collaborative Group and others 2015), can be dispensed safely to outpatients and are available as relatively low-cost generics (although even generic tamoxifen costs about US$15 per year in India, and generic AIs currently cost about US$50 per year). Chemotherapy also reduces recurrence but is more toxic and requires more careful medical supervision to ensure safety and efficacy. New drugs, for example, trastuzumab, that target other breast cancer receptors are not at present cost-effective in LMICs.

Relatively simple regimens of generic cytotoxic drugs (for example, four cycles of daunorubicin and cyclophosphamide with drug costs of about $200 in India) should be practicable wherever surgery is practicable (Anderson and others 2015), and could be offered to women who are otherwise in good health but whose disease has already spread from the breast to the local lymph nodes (Early Breast Cancer Trialists' Collaborative Group and others 2012). More effective cytotoxic regimens (for example, with taxanes) would increase toxicity, drug costs, and supervision costs.

Finally, global initiatives might well help to lower the cost of cancer drugs and other commodities, and develop and disseminate standardized resource-appropriate treatment protocols, such as those developed by the Breast Health Global Initiative. The successful global initiative to aid in the diagnosis and treatment of HIV/AIDS provides a model (Piot and Quinn 2013).

or treatment of schistosomiasis to prevent bladder or intestinal cancer in parts of Asia, the Middle East and North Africa, and Sub-Saharan Africa (IARC 1994). Finally, occupational hazards should be monitored and mitigated where necessary, for example, use of power tools on asbestos roofing or insulation, or heavy smoke pollution in houses (IARC 2012).

As important as what to include in a national cancer package is what to exclude. Cancer is notorious for exaggerated claims of causation (for example, nuclear power plants and folic acid) and claims of cure, even of advanced cancers and even within the health care system itself. A guidepost for the former category of claims is IARC's *Monographs on the Evaluation of Carcinogenic Risks to Humans*, which, since 1971, have evaluated more than 900 agents (http://monographs.iarc.fr/index.php). Treating advanced cancers—although a common practice in HICs—is expensive, often painful for patients, and usually futile. Countries should carefully examine the resource requirements and likely success of

such treatments in deciding not only which cancers to include in a package, but the appropriate interventions by stage. For advanced cancers with little possibility of cure, palliative care may be the best alternative.

COST-EFFECTIVENESS OF INTERVENTIONS

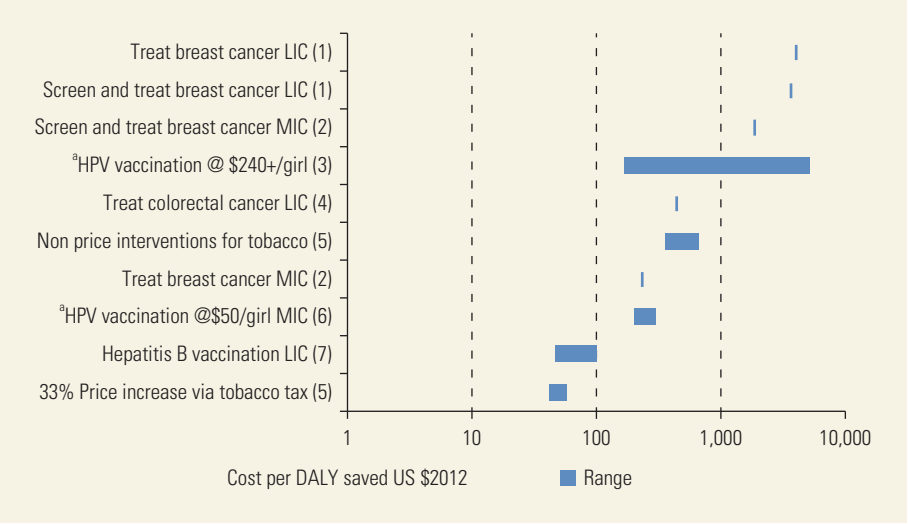
For most types of cancer, the cost-effectiveness literature for LMICs is slim (Horton and Gauvreau 2015, chapter 16 in this volume): nine studies were identified for breast cancer, two (plus four from high-income Asian countries) for colorectal cancer, one for liver cancer prevention, and none for pediatric cancer. Seventeen studies were sourced from an expert search for cervical cancer, and a recent systematic review of vaccines (Ozawa and others 2012) identified three studies for hepatitis B vaccination. A useful benchmark was to exclude from the essential package those interventions that are not clearly cost-effective in HICs. Most new drug treatments for advanced cancer fall in this category, such as bevacizumab (a monoclonal antibody) for metastatic breast cancer, which, at current prices, does not meet cost-effectiveness criteria in the United Kingdom (Rodgers and others 2011) and other HICs (Dedes and others 2009; Montero and others 2012). Similarly, cetuximab (a monoclonal antibody for metastatic colon and lung cancers) plus irinotecan (a relatively new treatment for colon cancer) are not currently considered cost-effective in the United Kingdom (Tappenden and others 2007).

Excise taxes on tobacco (US$1–US$150 per disability-adjusted life year [DALY] averted) and hepatitis B vaccination (less than US$100/DALY averted) are very cost-effective in all LMICs. Opportunistic cervical cancer screening and treatment of precancerous lesions are likely also to be very cost-effective in all LMICs. The cost-effectiveness of HPV vaccination depends crucially on vaccine cost, but at US$15/per girl vaccinated, HPV vaccination is likely to be very cost-effective in all LMICs. Some aspects of the treatment for early breast cancer are cost-effective wherever breast cancer surgery has been performed (mainly MICs; less than US$150/DALY averted) (figure 1.2).

COSTS OF PACKAGES

To provide per capita cost estimates for an essential package, we used available information on cost combined with demographic information from three large, diverse countries (Brazil, India, and Nigeria) (expressed in 2012 U.S. dollars). Although Nigeria is a lower-middle-income country, we used its demographic structure and lack of existing facilities and human resources to represent the scenario of LICs, mainly in Sub-Saharan Africa.

Figure 1.2 Cost-Effectiveness of Selected Interventions



Sources: (1) Zelle and others 2012; (2) Salomon and others 2012; (3) Insinga and others 2007; Praditsitthikorn and others 2011; Termrungruanglert and others 2012; (4) Ginsberg and others 2010; (5) Jha and others 2006; (6) Kawai and others 2012; Vanni and others 2012; (7) Prakash 2003; Griffiths, Hutton, and Das Dores Pascal 2005; Kim, Salomon, and Goldie 2007.

Note: Studies used for calculations were from a systematic search, whose findings are available online (annex 16A). Cost-effectiveness has not been calculated for elements of the essential package for which relevant data were entirely lacking. DALY = disability-adjusted life year; HPV = human papillomavirus; LIC = low-income country; MIC = middle-income country; QALY = quality-adjusted life year.

a. Based on a study reporting QALYs, not DALYs (the difference is small when interventions primarily reduce mortality).

To account for training, pathology services, and other system costs, we used a multiplier, equal to 50 percent of the intervention-based costs, drawn from similar costing studies for nutrition (Bhutta and others 2013) and health systems (Rao Seshadri and others 2015). However, we did not include the one-time investment costs for building hospitals, clinics, and other infrastructure that would eventually be needed to support cancer and other clinical services (Gospodarowicz and others 2015; Sloan and Gelband 2007).

The *DCP3* essential package of cancer control interventions would cost roughly an additional US$5.70 per capita in upper-middle-income countries, and US$1.70 per capita in both lower-middle-income countries and LICs (table 1.5). The annual cost of the essential package of cancer services (table 1.6) in 2013 dollars would be about US$13.8 billion, US$4.4 billion, and US$1.4 billion in those groups of countries, respectively. There are obvious caveats on the precision of the costs, including uncertainties of these costs by 2030. Importantly, drug costs can fall substantially as drugs go off patent, and global initiatives could further reduce the prices of key generic drugs and other commodities.

Table 1.5 Approximate Per Capita Marginal Costs of the Essential Package for Low-Income, Lower-Middle-Income, and Upper-Middle-Income Countries

(2012 U.S. dollars)

Intervention	Low-income	Lower-middle-Income	Upper-middle-income
Comprehensive tobacco control measures	0.05	0.07	1.06
Palliative care and pain control	0.05	0.06	0.06
HBV vaccination	0.08	0.04	0.04
Promote early diagnosis and treat early-stage breast cancer	0.43	0.43	1.29
HPV vaccination	0.23	0.23	0.40
Screen and treat precancerous lesions and early-stage cervical cancer	0.26	0.29	0.87
Treat selected childhood cancers	0.03	0.03	0.09
Subtotal	**1.13**	**1.15**	**3.81**
Ancillary services (50% of subtotal)	**0.57**	**0.58**	**1.91**
TOTAL COSTS	**1.70**	**1.73**	**5.72**

Source: Based on online annex 1A and Horton and Gauvreau 2015, annex 16A.
Note: HPV = human papillomavirus; HBV = hepatitis B virus.

Table 1.6 Resource Requirements for the Essential Cancer Intervention Package for LMICs

Expenditures	Low-income	Lower-middle income	Upper-middle income	Total LMICs
Public spending on health as % GDP, 2013	2.0	1.8	3.1	3.0
Total public spending on health in 2013 (US$ billions)	11	89	534	634
Required amount for cancer in 2013 (US$ billions)	1.4	4.4	13.8	19.6
Cancer package as % of total public spending on health in 2013[a]	13.0	4.9	2.6	3.1

Note: GDP = gross domestic product; LMICs = low- and middle-income countries.
a. Based on spending data from World Bank 2014b.

AFFORDABILITY AND DOMESTIC FINANCING OF ESSENTIAL CANCER SERVICES

The total estimated annual cost of the essential package of cancer interventions for all LMICs is about $20 billion dollars (2013 U.S. dollars). A useful metric is the cost of the package as a proportion of current total public spending on health. This is 2.6 percent in UMICs, 5 percent in lower-middle-income countries, and 13 percent in LICs. By comparison, HICs devote 3–7 percent of their total health spending to cancer control (OECD 2013). Most LMICs allocate far less; cancer currently accounts for about 1 percent of health spending (public and private) in Brazil and India, and 2 percent in China and Mexico (Goss and others 2013; IARC 2014; Knaul and others 2011).

Financing for cancer control will have to come mainly from national health care budgets, particularly in MICs, where rising incomes are enabling expansion of public financing for health (Jamison and others 2013; Knaul and others 2015, chapter 17 in this volume). South Africa, for example, has assessed which interventions it might include in an expanded national health insurance package (Shisana and others 2006) and similar work is underway in India (Jha and Laxminarayan 2009; Rao Seshadri and others 2015). In LICs, it would be inappropriate for governments to shift to spending 13 percent of their health care dollars on cancer. External assistance will be needed in those countries to establish an expansion path for cancer control.

A clear principle to adopt is the eventual goal of coverage for every person—even if coverage expands gradually—but not coverage of everything (WHO 2000), since poorly conceived plans may provide coverage of more expensive treatments for a few, while missing the opportunity to expand cost-effective population coverage. Public finance is not necessarily synonymous with public delivery (Musgrove 1996). Properly regulated private hospitals, facilities, and providers can be contracted to deliver cancer control interventions (Jha and Laxminarayan 2009).

Several countries in Latin America are already expanding their health insurance systems from coverage limited to occupational groups or selected vulnerable groups, to more comprehensive coverage (Goss and others 2013). However, for some lower-middle-income countries and most LICs, substantial increases in public finance for health, paired with economic growth or external assistance, would be needed to adopt a full package of interventions (Jamison and others 2013). Even those countries could benefit from considering the future cancer burden, costs, and financing to project a future cancer control plan. Higher tobacco taxes are the most important single cancer prevention intervention at a practical level, and a tripling of the excise tax on tobacco (thereby approximately doubling prices) could mobilize an additional US$100 billion worldwide in annual revenue (Jha and Peto 2014). For all LMICs, the epidemiologic dividend that accrues from a decreased burden of infectious disease should generate savings that can be spent on NCD control (Jamison and others 2011).

IMPLEMENTATION CHALLENGES FOR THE ESSENTIAL PACKAGE

Within the essential package, some aspects of interventions may be implemented reasonably quickly, notably tobacco control measures that involve taxation and regulation (Jha and others 2015) and policy changes to increase access to opioids (although establishing nationwide programs and training a full cadre of providers may take years) (Cleary, Gelband, and Wagner 2015). Some interventions can be scaled to reasonably high coverage quickly with existing infrastructure, such as school-based HPV vaccination for adolescent girls, or hepatitis B vaccination for newborns. By contrast, other interventions will need expanded clinical access, most notably surgical treatment of early-stage breast cancer and cervical cancer (Dare and others 2015, chapter 13 in this volume). Increasing surgical capacity is relatively expensive but feasible from an organizational perspective, especially if existing district hospitals can be strengthened (Mock and others 2015) (paired with central cancer clinical expertise). When high quality surgery becomes available, early-stage, resectable tumors of various types, in addition to breast and cervical lesions, can be removed. Expanding chemotherapy treatment requires an extensive network of laboratories and follow-up, which in LICs and lower-middle-income countries is currently feasible only in urban areas. Scaling up radiotherapy requires large capital expenditures, and substantial attention to clinical guidelines and treatment protocols as well as safety assurances (Jaffray and Gospodarowicz 2015, chapter 14 in this volume).

Particularly for LICs where minimal cancer services exist in the public sector, the needed expertise and resources for cancer treatment will require years of steady investment to expand physical and human infrastructure. Elements that are missing or in short supply in LMICs (Bray and others 2014; Dikshit and others 2012; Gospodarowicz and others 2015) include trained professionals in oncology and relevant disciplines; appropriately-equipped facilities, including radiotherapy facilities, pathology services, and other laboratory testing services (for example, estrogen-receptor testing for breast

cancer tissue; box 1.3); supplies, including chemotherapy drugs; geographic access to facilities with affordable cancer services, including surgery; public awareness of the availability and effectiveness of cancer control interventions; and cancer incidence and cause-of-death data. As more people are successfully treated and live for many years, survivorship services (for example, rehabilitation, remedies for physical deficits caused by treatment, limiting the social stigma associated with having had cancer, and follow-up for recurrence) will increase in importance (Hewitt, Greenfield, and Stovall 2005), but costs for survivorship are not included in our estimates.

The package emphasizes treatment for *early-stage* cervical and breast cancers (and similarly, early stages for other cancers included in specific country plans), because cure rates are substantially higher than they are for more advanced cancers. Surgery is particularly important, as surgery alone is curative for many early cancers. Although locally appropriate cervix screening, which will identify many precancers and early cancers, is included in the package, there is no corresponding screening intervention for breast cancer. Even without screening, however, LMICs might be able to achieve a somewhat earlier stage of presentation of common cancers by making affordable treatment available and communicating this to people. Historical evidence from HICs, illustrated by stage-shifting for cervix cancer in Sweden before organized screening began around 1960, supports this approach (Pontén and others 1995).

Cancer treatment can be organized through existing medical facilities (particularly district hospitals) or through specialized centers, but the key is to ensure good links between facilities (Sloan and Gelband 2007), which requires a centralized locus of control and the ability to adjust elements of the system that are not working to the benefit of patients (Gospodarowicz and others 2015). An example from childhood cancer illustrates this well. All children with cancer in Honduras (population 8 million) are treated in two centers that collaborate and communicate closely (Metzger and others 2003). In contrast, children with cancer in Colombia (population 48 million) are treated in more than 150 health care institutions of varying size, with little to no communication between centers (Gupta and others 2015). This adversely affects patient outcomes and costs. India, population 1.3 billion, faces more challenging coordination of care, but is building a National Cancer Grid (Pramesh, Badwe, and Sinha 2014) linking non-specialist hospitals to specialist cancer centers and providing them with current treatment protocols.

Building and improving a nation's cancer control capacity requires attention to the quality of services, from pathology and diagnosis to surgery, chemotherapy, radiotherapy, and palliative care (Gospodarowicz and others 2015). Upgrading hospitals to provide basic cancer surgical services (Mock and others 2015), developing cancer referral networks, tracking service performance, integrating the delivery of different types of services, and ensuring that financial flows accompany services are also required.

GLOBAL INITIATIVES FOR CANCER CONTROL

Only 1 percent of the US$30 billion development assistance for health in 2010 was allocated to NCDs, only a portion of which was for cancer (IHME 2012). NCD funding is likely to increase somewhat with increasing global recognition of the importance of NCDs. However, it is unlikely that significant global funds will be allocated to support national health systems to deal with cancer. As additional funding becomes available, we suggest three priorities for international support.

1. *Lower the costs to countries of key inputs for the essential package and other cost-effective interventions, such as HPV and other vaccines, cancer drugs (including generics), screening tests (for example, HPV tests), laboratory reagents and other test commodities, surgery, radiotherapy machines, and other relevant goods.* The Global Fund for AIDS, TB and Malaria; Gavi; the Clinton Health Access Initiative; and other international partnerships have developed mechanisms to reduce the price of a range of global commodities relevant to infectious disease control, utilizing economies of scale (relevant for purchases of drugs or radiotherapy machines), subsidies for reputable and affordable medicines, advanced market commitments, and similar innovations (Piot and Quinn 2013). Similar efforts for cancer are possible, for example, as has been proposed for radiotherapy by the Global Task Force on Radiotherapy for Cancer Control (Union for International Cancer Control [UICC]).
2. *Expand technical assistance in cancer control.* International and regional networks exist for many aspects of cancer care, such as treatment guidelines; networks on breast, cervical, and colorectal cancer screening; childhood cancer treatment and research; and palliative care. Other support modalities, for example, twinning institutions, have typically involved institutions in HICs and LICs (North-South collaborations), but as in other areas, the opportunities should grow to add South-South collaborations. Within countries, peer-based and professional standards of cancer care and reporting of outcomes and performance for various facilities

can improve quality of care (Peabody and others 2006; Varmus and Trimble 2011).

3. *Support for research* is a worthwhile investment for overseas developmental assistance. Research priorities include tracking national cancer burdens, clinical trials, and implementation science, including research on delivery systems; cancer epidemiology and biology; widely practicable, low-cost technologies; and economics (Trimble and others 2015, chapter 15 in this volume).

BENEFITS OF EXPANDED CANCER CONTROL

Despite substantial challenges in most LMICs, appreciable reductions in the cancer burden might well be possible by 2030, with even greater reductions by 2050 and beyond (Norheim and others 2014), particularly through treating common cancers that are detected early, tobacco control that encourages widespread adult smoking cessation, and vaccination against hepatitis B and HPV.

Global cancer death rates at ages 0–69 years were declining at about 10 percent per decade during 2000–10. If this were to continue, then from 2010 to 2030 cancer death rates will fall by almost 20 percent. A decrease of one-third in global cancer death rates by 2030, as proposed recently (Norheim and others 2014), would require faster progress in LMICs, particularly marked increases in tobacco cessation. The WHO estimates that tobacco control, HPV and HBV vaccination, and opportunistic cervical cancer screening could avoid about 6 percent of cancer deaths by 2030 (or about 200,000 deaths before age 70 years annually). The *DCP3* essential package could achieve greater reductions. If, as expected, the availability of treatment shifts diagnoses for common, treatable cancers to earlier stages, further lives could be saved. The benefits of pain relief are not measured in lives saved, but are important.

Finally, cancer control contributes to reduced inequality in health, providing relatively larger benefits to the poor. In China, increased tobacco taxes and access to cervical cancer prevention, such as screening and HPV vaccination, would disproportionately benefit those in the lowest income quintile by reducing deaths and through better financial risk protection from catastrophic health expenditures (Levin and others 2015, chapter 18 in this volume; Verguet and others 2015).

Cancer control is often approached with pessimism, but practicable, deliberate, cost-effective steps can enable many countries to reduce substantially by 2030 the suffering and premature death from cancer, with much greater improvements by 2050.

NOTES

Maps and figures in this chapter are based on incidence and mortality estimates for ages 0–69, consistent with reporting in all *DCP3* volumes. The discussion of burden (including risk factors) and interventions, however, includes all ages unless otherwise noted.

The World Bank classifies countries according to four income groupings. Income is measured using gross national income per capita, in U.S. dollars, converted from local currency using the World Bank Atlas method. Classifications as of July 2014 are as follows:

- Low-income countries = US$1,045 or less in 2013
- Middle-income countries are subdivided:
  - Lower-middle-income = US$1,046–US$4,125
  - Upper-middle-income = US$4,126–US$12,745
- High-income countries = US$12,746 or more

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